AMENDMENTS TO THE CLAIMS:

Please enter the following amendments into the subject application.

1. (**Currently Amended**) A transgenic mouse ~~or rat~~ comprising a polynucleotide encoding a human C5aR or humanized C5aR,wherein the C5a endogenous to the mouse ~~or rat~~ binds to and effects signalling of the human or humanized C5aR**, and wherein the transgenic mouse is homozygous for the polynucleotide encoding a human or humanized C5aR.**

2. (**Currently Amended**) The transgenic mouse ~~or rat~~ according to claim 1, wherein the polynucleotide encodes human C5aR comprising a sequence as shown in SEQ ID NO:3, or an allelic variant thereof.

3. (**Currently Amended**) The transgenic mouse ~~or rat~~ according to claim 1, wherein the polynucleotide comprises a sequence as shown in SEQ ID NO:2, or an allelic variant thereof.

4. (**Currently Amended**) The transgenic mouse ~~or rat~~ according to claim 1, wherein the polynucleotide encodes humanized C5aR.

5. (**Currently Amended**) The transgenic mouse ~~or rat~~ according to claim 4, wherein the humanized C5aR comprises a C5aR sequence endogenous to the mouse ~~or rat~~ wherein at least one extracellular or intracellular domain is replaced with the corresponding human C5aR domain.

6. - 9. (Cancelled)

10. (**Currently Amended**) The transgenic mouse ~~or rat~~ according to claim 1, wherein the endogenous C5aR coding sequence or a fragment thereof has been replaced with a corresponding human C5aR coding sequence or fragment thereof ~~by way of targeted homologous recombination~~.

11. – 13. (Cancelled)

14. (**Currently Amended**) [[The]] **An** isolated cell(s), cell line, tissue or organ obtained from the transgenic mouse ~~or rat~~ of claim 1, the isolated cell, cell line, tissue or organ comprising a polynucleotide encoding a human C5aR or humanized C5aR.

15. (**Currently Amended**) A method for producing a transgenic mouse ~~or rat~~ for testing compounds for an effect on a phenotype associated with C5aR signalling, the method comprising introducing into the genome of a mouse ~~or rat~~ a polynucleotide construct encoding human C5aR, humanized C5aR or a fragment of human C5aR, to produce a transgenic mouse ~~or rat~~**, wherein the C5a endogenous to the mouse binds to and effects signalling of the human or humanized C5aR,**.

16. (Previously presented) The method according to claim 15, wherein the polynucleotide construct encodes human C5aR.

17. (Previously presented) The method according to claim 16, wherein the polynucleotide construct encodes a polypeptide comprising a sequence as shown in SEQ ID NO:3, or an allelic variant thereof.

18. (Previously presented) The method according to claim 16, wherein the polynucleotide construct comprises a sequence as shown in SEQ ID NO:2, or an allelic variant thereof.

19. (Previously presented) The method according to claim 15, wherein the polynucleotide construct encodes humanized C5aR.

20. (Previously presented) The method according to claim 15, wherein the polynucleotide construct encodes a fragment of human C5aR.

21. (Cancelled)

22. (Previously presented) The method according to claim 20, wherein the fragment encompasses at least one extracellular domain of human C5aR.

23. - 26 (Cancelled)

27. **(Currently Amended)** The method according to claim 15, wherein the method comprises replacing the endogenous C5aR coding sequence or a fragment thereof with a corresponding human C5aR coding sequence or fragment thereof ~~by way of targeted homologous recombination~~.

28. (**Currently Amended**) A method for evaluating at least one pharmacokinetic and/or pharmacodynamic effect of a candidate compound, the method comprising administering a candidate compound to a transgenic mouse ~~or rat~~ according to claim 1 or isolated tissue or cells obtained therefrom, and examining at least one pharmacokinetic and/or pharmacodynamic effect of the candidate compound on the transgenic mouse ~~or rat~~ **or isolated tissue or cells obtained therefrom**.

29. (Cancelled)

30. (Previously presented) The method according to claim 28, wherein the at least one pharmacokinetic effect examined is volume of distribution, total clearance, protein binding, tissue binding, metabolic clearance, renal clearance, hepatic clearance, biliary clearance, intestinal absorption, bioavailability, relative bioavailability, intrinsic clearance, mean residence time, maximum rate of metabolism, Michaelis-Menten constant, partitioning coefficients between tissues and blood or plasma, fraction excreted unchanged in urine, fraction of drug systemically converted to metabolites, elimination rate constant, half-life, or secretion clearance.

31. (Previously presented) The method according to claim 28, wherein the at least one pharmacodynamic effect is modulation of a phenotype associated with C5aR signalling.

32. (**Currently Amended**) The method according to claim 31, the method comprising

(i) administering a candidate compound to a transgenic mouse ~~or rat~~ comprising a polynucleotide encoding a human C5aR or humanized C5aR, or isolated tissue or cells obtained therefrom, under conditions in which at least one phenotype associated with C5aR signalling is expressed; and

(ii) monitoring development of the at least one phenotype following administration of the compound.

33. (**Currently Amended**) The method according to claim 32, wherein the method further comprises (iii) comparing the extent of the phenotype in the transgenic mouse ~~or rat~~ or cells derived therefrom to which the compound was administered relative to a control mouse ~~or rat~~ or cells derived therefrom, wherein any difference in the nature or extent of the phenotype when compared to the control mouse ~~or rat~~ indicates the potential of the compound to modulate C5aR activity.

34. (**Currently Amended**) The method according to claim 31, the method comprising (i) administering a candidate compound to a transgenic mouse ~~or rat~~ or isolated tissue or cells obtained therefrom under conditions in which at least one phenotype associated with C5aR signalling is expressed; (ii) monitoring development of the at least one phenotype following administration of the compound; and (iii) comparing the extent of the phenotype in the transgenic mouse ~~or rat~~ to which the compound was administered relative to a control mouse ~~or rat~~ , wherein any reduction or inhibition in the nature or extent of the phenotype when compared to the control mouse ~~or rat~~ indicates the potential of the compound to inhibit or reduce C5aR activity.

35. (**Currently Amended**) The method according to claim 31, the method comprising (i) administering a candidate compound to a transgenic mouse ~~or rat~~ or isolated tissue or cells obtained therefrom under conditions in which at least one phenotype associated with C5aR signalling is expressed; (ii) monitoring development of the phenotype following administration of the compound; and (iii) comparing the extent of the phenotype in the transgenic mouse ~~or rat~~ to which the compound was administered relative to a control mouse ~~or rat~~ , wherein any enhancement in the nature or extent of the phenotype when compared to the control mouse ~~or rat~~ indicates the potential of the compound to promote or enhance C5aR activity.

36. - 39. (Cancelled)

40. (Previously presented) The method according to claim 28 wherein the compound is selected from the group consisting of: a peptide, including a peptide derived from C5aR or C5a or other non-C5aR peptide and capable of inhibiting, reducing or repressing a C5aR function, a C5aR dominant-negative mutant; a non peptide inhibitor of C5aR; an antibody or antibody fragment which binds to C5aR and inhibits a C5aR function; a small organic molecule, a nucleic acid encoding said peptide derived from C5aR or C5a or other non-C5aR peptide inhibitor, an antisense nucleic acid directed

against C5aR-encoding mRNA, an anti-C5aR ribozyme, and a small interfering RNA (RNAi) that targets C5aR gene expression.

41. (Cancelled)